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Antimicrobial Susceptibility Pattern of *Staphylococcus aureus*

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Abstract

Staphylococcus aureus particularly methicillin-resistant *Staphylococcus aureus* (MRSA) strains is one of the major causes of community and hospital-acquired bacterial infections. They are also becoming increasingly multidrug resistant and recently developed resistance to vancomycin, which has been used successfully to treat MRSA for many years. In vitro determination of drug resistance patterns of *S. aureus* is critical for the selection of effective drugs for the treatment of staphylococci infections. The main aim of this review was to determine the prevalence of drug-resistant *S. aureus* strains from different clinical specimens throughout the world. Various types of research study designs such as cross-sectional and retrospective and laboratory techniques like Kirby Bauer, agar dilution, and E tests were used. The result of each study was narrated accordingly.

Keywords: prevalence, MRSA, beta-lactamase, antimicrobial susceptibility pattern

1. Introduction

Staphylococcus aureus particularly methicillin-resistant *Staphylococcus aureus* (MRSA) strains is one of the major causes of community and hospital-acquired bacterial infections. They are also becoming increasingly multidrug resistant and recently developed resistance to vancomycin, which has been used successfully to treat MRSA for many years. In vitro determination of drug resistance patterns of *S. aureus* is critical for the selection of effective drugs for the treatment of staphylococci infections. The main aim of this review was to determine the prevalence of drug-resistant *S. aureus* strains from different clinical specimens throughout the world. Different types of research study designs such as cross-sectional and retrospective and laboratory techniques like Kirby Bauer, agar dilution, and E tests were used. The result

of each study was narrated with respect to antimicrobial susceptibility pattern of *S. aureus* to various drugs accordingly.

A study on methicillin resistance against *S. aureus* in Trinidad and Tobago was conducted by Akpaka et al. [1]. Of 1912 *S. aureus* isolates recovered from different clinical samples, 12.8% were found out to be methicillin (oxacillin) resistant. The highest (86%) of the isolates were obtained from wound swabs and the least from urine (0.4%) specimens. About 85% of methicillin-susceptible *S. aureus* (MSSA) were sensitive to commonly used antimicrobials in the country. On the other hand, all MRSA isolates were resistant to ceftriaxone, erythromycin, gentamycin, and penicillin but were 100% sensitive to vancomycin, rifampin, and chloramphenicol.

Similar study was carried out by Orrett and Land [2] in Trinidad and Tobago. In this study, 2430 isolates of *S. aureus* strains recovered from various clinical sources, from hospital and community practices, were analyzed. The prevalence of MRSA varied with the type of clinical sample. The prevalence of MRSA from surgical/burn wound was the highest (60.1%) followed by urine (15.5%) and pus/abscess (6.6%), respectively. The prevalence of MSSA also varied with the type of clinical samples. The major sources of MSSA were surgical/burn wounds, pus/abscess, and upper respiratory tract specimens with rates of 32.9, 17.1, and 14.3%, respectively. Furthermore, 109 (4.5%) *S. aureus* strains were isolated from sputum, 201(8.3%) from blood, and 95(4%) from eye infection. Clinical specimens each accounting less than 3% of the total include the vagina, ear, and CNS. With regard to the antimicrobial susceptibility profile of the isolates, the greatest prevalence of resistance of MRSA was seen for erythromycin (86.7%) and clindamycin (75.3%). Resistance rates among MSSA were highest for ampicillin (70%).

Oxacillin-resistant and multidrug-resistant *Staphylococcus aureus* in Lima, Peru, was studied by Seas et al. [3]. *S. aureus* isolates were recovered from the blood, sterile body fluids (e.g., cerebrospinal fluid, peritoneal, joint, and pericardial fluids), urine, skin and soft tissue, lungs, abscesses, surgical wound sites, and catheters. Of 103 strains isolated, 70 (68%) were MRSA. In the United States, the prevalence of MRSA in skin and soft tissue infections was conducted by Frazee et al. [4]. Among 137 study subjects, 119 *S. aureus* isolates were recovered of which MRSA was present in 51% of infection site cultures. Of 119 isolates 89 (75%) were MRSA. All MRSA strains were susceptible to trimethoprim/sulfamethoxazole, 94% to clindamycin, 86% to tetracycline, and 57% to levofloxacin. Similarly, results of this study revealed that the prevalence of MRSA was 59%. Moran et al. [5] conducted MRSA prevalence study in patients with skin and soft tissue infections. In this study a total of 422 patients with skin and soft tissue infections were enrolled. *S. aureus* was isolated from skin and soft tissue infection in 320 (76%) patients of which 249 (78%) of the *S. aureus* isolates were MRSA. This study revealed that the isolation rate of MRSA varies with respect to clinical sample. MRSA isolated from abscesses, purulent wounds, and cellulitis with purulent exudates accounted 61, 53, and 47%, respectively.

The prevalence of MRSA across the European countries from 1999 to 2002 was analyzed by Tiemersma et al. [6]. In this study a total of 50,759 *S. aureus* isolates were collected from 495 hospitals in 26 countries. The prevalence of MRSA varied from 1% in Northern Europe to 40% in Southern and Western Europe. The study also has shown that the prevalence of MRSA

increased significantly in countries such as Belgium, Germany, Ireland, the Netherlands, and the United Kingdom, while the prevalence of MRSA showed a decrease in Slovenia. In addition this study revealed that MRSA was more frequently isolated from men than women and patients with blood culture positive for MRSA were older than patients with MSSA.

Many studies on the prevalence of MRSA have been conducted in India. A total of 1426 wound swabs were taken from 450 high-risk patients by Vidhani et al. [7] of which *S. aureus* was isolated from 188 patients (41.8%) and out of which 97 (51.6%) patients were found to be MRSA. A marked difference in antibiotic sensitivity pattern of MRSA and MSSA isolates was reported. According to the results of this study, none of the MRSA isolate was found to be sensitive to penicillin and amoxicillin. However, 6 (5.5%) and 12 (11%) MSSA were sensitive to penicillin and amoxicillin. A total of 85 (77.9%) of MSSA were sensitive to cefotaxime, while only 17 (21.5%) of MRSA were sensitive to this antibiotic. Sensitivity to macrolide group of antibiotics like erythromycin and roxithromycin was seen in 77 (70.6%) of MSSA in comparison to 14 (17.7%) of MRSA. Susceptibility test results of this study further showed that among the aminoglycosides maximum sensitivity of MSSA was seen with amikacin 74 (67.9%), while only 21 (26.6%) of MRSA were sensitive to the same antibiotic. A total of 53 (67%) of MRSA and 76 (69.7%) of MSSA were found to be sensitive to fluoroquinolone group, that is, ofloxacin. All *S. aureus* isolates (MRSA and MSSA) were found to be uniformly sensitive to vancomycin which is the drug of choice for treating infections caused by MRSA.

Another study conducted by Rajendra Goud et al. [8] revealed a prevalence 29.76% of community-associated MRSA. All community-associated MRSA were resistant to methicillin and penicillin, while resistance to erythromycin and vancomycin was 65 and 1.12%, respectively, but all MRSA isolates were sensitive to linezolid. A third study conducted by Sharma and Mall [9] found out that out of 200 nasal samples, *S. aureus* was recovered from 97 patients, and of these, 23 isolates were MRSA. The drug resistance patterns of MRSA isolated from clinical specimens, and carrier screening samples were found to be highly variable. Almost all the MRSA strains (91.3%) screened from nasal samples were resistant to amikacin, 86.95% to kanamycin and cloxacillin, 78.26% to ciprofloxacin, 56.52% to erythromycin, 52.17% to chloramphenicol, and 34.78% to both tetracycline and gentamycin. The production of β -lactamase enzyme in MRSA was found to be 19 (82.6%). Chandrashekhara et al. [10] isolated 312 *S. aureus* strains of which 177 (56.75%) were found to be MRSA. Susceptibility profile of this study showed that all MRSA were resistant to penicillin, followed by erythromycin (91.5%), ampicillin+ sulbactam (90.4%), amoxicillin (83.6%), norfloxacin (81.4%), cefuroxime (78.5%), and amikacin (25.4%). However, no strains were resistant to vancomycin. Similar study carried out by Kaur et al. [11] revealed that 27 out of 70 (38.6%) *S. aureus* isolates were MRSA.

A number of similar studies were carried out in other Asian countries. A study carried out in Tehran by Vahdani et al. [12] exhibited marked variation in the drug susceptibility of MRSA. The results of this study showed that all the 90 MRSA isolates were resistant to penicillin (100%), ampicillin (92%), and cefotaxime (93%). Vancomycin and chloramphenicol were the most effective antibiotics, and only 7 and 14% of isolates were resistant, respectively. Nitrofurantoin, gentamycin, amikacin, ciprofloxacin, and other cephalosporins like cefepime and cefazolin were better active than penicillin, ampicillin, and cefotaxime. This study showed that 44% of hospital-acquired MRSA strains were resistant to co-trimoxazole. Akhter et al. [13]

in Karachi isolated MRSA and determined the drug susceptibility of pattern of both MRSA and MSSA. A total of 87 strains of *S. aureus* were recovered from various clinical samples by the authors. Of these, 66 (75.8%) strains were recovered from various swabs and 21 (24.13%) from blood. Of the isolates 20 (22.9%) were methicillin resistant. In this group high resistance was found to cloxacillin (100%), co-trimoxazole (95%), erythromycin (70%), and gentamicin (55%), and low resistance was observed to ciprofloxacin (30%). In MSSA 0% resistance was seen to ciprofloxacin and chloramphenicol, and high resistance was found to co-trimoxazole (98.5%) and penicillin (73.13%). Both MRSA and MSSA were 100% sensitive to vancomycin. A total of 139 MRSA were isolated by Kaleem et al. [14] in Pakistan. Of this most of the MRSA were isolated from pus samples. As far as their drug susceptibility is considered, all of the isolated MRSA were found to be susceptible to vancomycin and linezolid. Furthermore, 130 isolates (94%) were susceptible to teicoplanin and minocycline, whereas 93% of isolates were sensitive to chloramphenicol and 91% were sensitive to tetracycline. Only 38 and 22% of the isolates were susceptible to fluoroquinolones and macrolides, respectively.

A good number of research work on the prevalence, rate of isolation, and drug susceptibility profile of MRSA have been carried out in Africa. A study carried out by Ojulong et al. [15] investigated 188 pus swabs collected from patients with surgical site infections. Out of 54 (28.7%) *S. aureus* isolates, 17 (31.5%) were found out to be MRSA. Resistance rates of MRSA were found out to be 88.2% for trimethoprim-sulfamethoxazole, 88.2% for erythromycin, 58.8% for gentamycin, 70.6% for ciprofloxacin, and 88.2% for chloramphenicol, and all MRSA isolates were found to be sensitive to vancomycin and clindamycin. A study carried out in Sudan by Alamin et al. [16] recovered 85 *S. aureus* strains of which 21 (24%) were isolated from nasal cavity, 26 (31%) from skin surface, 22 (26%) from wounds, and 16 (19%) from the throat. Out of 85 isolates, 25 were found out to be MRSA.

Okwu et al. [17] in Nigeria examined 120 samples taken from the nose. Of these 22 (18.3%) were found to be positive for *S. aureus*, and 13 (10.8%) of the isolates were oxacillin resistant. Their studies also depicted that seven (11.7%) MRSA strains were obtained from females, while six (10%) strains were from males. Also, 12 (19.4%) *S. aureus* and 7 (11.3%) MRSA were isolated from the age group of 9–14 years, while 10 (17.3%) isolated of which 6 (10.3%) were MRSA isolated the age groups of 3–8 years. Furthermore, the isolates were resistant to ampicillin (100%), cloxacillin (100%), penicillin (100%), tetracycline (82%), chloramphenicol (73%), erythromycin (68%), gentamicin (64%), streptomycin (56%), and oxacillin (55%). Another study conducted by Olowe et al. [18] in the same country, Nigeria, depicted that out of 67 *S. aureus* isolates, 32(47.8%) were resistant to methicillin. High prevalence of MRSA, 13 (19.4%), was isolated from wound, while urine sample had the least, 1(1.5%). High resistance levels (87.5%) were detected against penicillin and tetracycline, while gentamicin and vancomycin recorded the least resistance levels of 62.5 and 6.3%, respectively. The starch paper analysis confirmed the presence of beta-lactamase production in all the isolates tested (100%). Similar study was conducted to detect beta-lactamase production in the same country by Efuntoye et al. [19]; of the 95 isolates tested. A total of 79 (83.2%) were beta-lactamase-producing strains.

In Ethiopia, a retrospective study on the prevalence of MRSA was conducted by Geyid et al. [20]. The results of this study showed that among 249 *S. aureus* isolates 75 (30.5%) were found

out to be MRSA, while 173 (69.5%) were MSSA. With regard to antibiotic susceptibility pattern of the isolates, vancomycin and clindamycin were effective against all *S. aureus* isolates. The presence of beta-lactamase production was determined in the 355 *S. aureus* isolates, and 252 (71%) were found to be beta-lactamase producers. Furthermore, 47 (62%) of the MRSA isolates and 140 (81%) of the MSSA isolates were beta-lactamase-positive strains. The sensitivity pattern of all the *S. aureus* isolates against 11 common drugs indicated that the majority (80%) of the MRSA strains were multidrug resistant, while 4 (8%) were not resistant to any of the drugs tested. A total of 41 (54%) MRSA strains were both beta-lactamase producers and multidrug-resistant isolates. Another study carried out in Felege Hiwot Referral Hospital, Bahir Dar, showed that 55% of *S. aureus* isolates were MRSA [21].

Similarly, in a study conducted by Dilnessa et al. [22], of 1360 clinical specimens analyzed, *S. aureus* was recovered from 194 (14.3%). Rate of isolation of *S. aureus* with regard to clinical specimens was the highest in pus 118 (55.4%). No *S. aureus* was isolated from CSF and urethral discharge. Out of 194 *S. aureus* isolates, 34 (17.5%) were found out to be MRSA and the remaining 160 (82.5%) were MSSA. A total of 98 (50.5%) *S. aureus* isolates were multidrug resistant, and the highest isolates were resistant to penicillin 187 (96.4%) and least resistant for clindamycin 23 (11.9%) and vancomycin 10 (5.1%). MRSA strains were 100% resistant to penicillin G, erythromycin, and trimethoprim-sulfamethoxazole and least resistant to vancomycin 10 (29.4%). Out of 194 *S. aureus* isolates, 153 (79.0%) were beta-lactamase producers (Table 1).

Factors that could contribute to variations in the prevalence rate of MRSA and vancomycin could be due to differences in the length of study period, number of study sites, sample size,

Authors (publication year)	Country	Sample size	No. of <i>S. aureus</i> (N/%)	MRSA (N/%)	MSSA (N/%)	VRSA (%)	MDRSA (%)
Moran et al. (2006)	USA	422	320 (76)	249 (78.0)	71 (22.0)	—	—
Ojulong et al. (2009)	Uganda	188	54 (28.7)	17 (31.5)	37 (68.5)	0	—
Sharma and Mall (2011)	India	200	97 (48.5)	23 (23.7)	74 (76.3)	—	—
Okwu et al. (2012)	Nigeria	120	22 (18.3)	13 (59.1)	9 (40.9)	—	100
Akpaka et al. (2006)	Spain	—	1912	244 (12.8)	1668 (87.2)	0	—
Geyid et al. (1991)	Ethiopia	17,142	249 (1.4)	76 (30.5)	173 (69.5)	0	80
Dilnessa et al. (2016)	Ethiopia	1360	194 (14.3)	34 (17.5)	160 (82.5)	5.1	50.5
Olowe et al. (2012)	Nigeria	—	67	32 (47.8)	35 (52.2)	6.3	100
Vidhani et al. (2000)	India	450	188 (41.7)	97 (51.6)	91 (48.4)	—	79.5
Alamin et al. (2013)	Malaysia	—	85	25 (29.4)	60 (70.6)	8	—

MRSA, Methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; MDRSA, multidrug-resistant *S. aureus*; VRSA, vancomycin-resistant *S. aureus*

Table 1. Comparison of different literatures with respect to methicillin- and vancomycin-resistant pattern of *Staphylococcus aureus* in different countries.

and sample type, and the lab procedures employed can be mentioned. The isolates were multidrug resistant to several combinations of the tested antibiotics. According to Magiorakos et al. [23], MDR is defined as non-susceptibility to at least one agent in three or more antimicrobial categories. Over all drugs such as gentamicin, amoxicillin-clavulanate, clindamycin, cefuroxime, vancomycin, and cephalothin had relatively lower resistance.

2. Conclusion

The prevalence of *S. aureus* and MRSA varies appreciably based on the type of clinical samples. Pus is the main source of *S. aureus* and MRSA than other samples in hospital settings. The prevalence of MRSA strains obtained from different studies varies based on geographical location. Many MRSA strains were multidrug resistant, and a good number of the isolates were also resistant to vancomycin, the drug of choice for treating multidrug-resistant MRSA infections. Reducing this burden by good infection control practices such as strict hand washing, by identifying MRSA carriers, and treating them, the prudent use of antimicrobial agents is recommended. Beta-lactamase production plays a great role for acquisition of MRSA. Physicians should prescribe drugs after the sensitivity pattern of the microbe is known. Additionally, large-scale longitudinal study is needed to determine CA-MRSA and HA-MRSA. Further phenotypic and genotypic studies are needed to establish and clarify the genetic mechanism behind susceptibilities to antibiotics.

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